



EXPLORING THE MOLECULAR AFFINITIES OF BENZIMIDAZOL: A MOLECULAR DOCKING STUDY

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ABSTRACT

Benzimidazole derivatives have garnered significant attention in medicinal chemistry due to their diverse pharmacological activities. In this project, molecular docking simulations were conducted to explore the binding affinities and interactions of benzimidazole derivatives with target proteins implicated in various diseases. The study employed computational techniques to predict the binding modes of benzimidazole derivatives against selected protein targets, including enzymes, receptors, and transporters. Through molecular docking analysis, key interactions such as hydrogen bonding, hydrophobic interactions, and π - π stacking were elucidated, providing insights into the structural requirements for favorable binding. The results of this study contribute to the understanding of the molecular mechanisms underlying the biological activities of benzimidazole derivatives, thereby facilitating rational drug design and optimization efforts in the development of novel therapeutic agents. This project focuses on the molecular docking investigation of benzimidazole with the protein target 1kzn. Utilizing computational techniques, the study aims to elucidate the potential binding affinity and interaction patterns between benzimidazole and the specified protein target. By analyzing the docking results, insights into the molecular recognition and binding mechanisms of γ with protein 1kzn were obtained. This research provides valuable information for understanding the pharmacological relevance of benzimidazole derivatives and aids in rational drug design strategies targeting protein 1kzn for therapeutic interventions.

INTRODUCTION

Benzimidazole and its derivatives represent a class of compounds with remarkable pharmacological potential, attracting considerable interest in drug discovery and development efforts. The unique structural features of benzimidazole, characterized by a bicyclic heterocyclic ring system, offer a versatile scaffold for the design of bioactive molecules targeting diverse biological pathways. This introduction sets the context for exploring the molecular docking of benzimidazole and its derivatives, highlighting their significance in medicinal chemistry research. Benzimidazole compounds have garnered attention across various therapeutic areas, including anticancer, antiviral, antibacterial, antifungal, antiparasitic, and anti-inflammatory applications. This broad spectrum of pharmacological activities stems from the ability of benzimidazole derivatives to interact with specific molecular targets within biological systems. By modulating the function of enzymes, receptors, ion channels, and transporters, benzimidazole-based agents exert their therapeutic effects through intricate molecular mechanisms. The process of molecular docking serves as a valuable computational tool in rational drug design, facilitating the prediction of ligand-receptor interactions and the exploration of binding modes at the atomic level. Through molecular docking simulations, researchers can assess the binding affinity and orientation of small molecules, such as benzimidazole derivatives, within the binding sites of target proteins. This predictive approach enables the identification of potential lead compounds and optimization of their pharmacological properties prior to experimental validation. In this project, the focus is on elucidating the molecular interactions between benzimidazole and selected protein targets using molecular docking techniques. By employing state-of-the-art computational methods, the aim is to uncover the structural basis of benzimidazole binding to specific protein targets implicated in disease pathways. Understanding the molecular recognition patterns and key intermolecular interactions will provide valuable insights into the pharmacological mechanisms underlying the bioactivity of benzimidazole derivatives. The outcome of this project holds significant implications for drug discovery and development efforts, offering opportunities to design novel benzimidazole-based therapeutics with enhanced potency, selectivity, and pharmacokinetic profiles. By leveraging computational modeling approaches, researchers can expedite the identification and optimization of lead compounds, ultimately advancing the discovery of innovative

treatments for various human diseases. In summary, the molecular docking of benzimidazole represents a promising avenue for exploring its pharmacological potential and elucidating its molecular interactions with target proteins. Through interdisciplinary research efforts combining computational and experimental approaches, this project aims to contribute to the development of next-generation benzimidazole-based therapeutics with clinical relevance and therapeutic efficacy.^[1]

MOLECULAR DOCKING

In the meadow of molecular modeling, docking is a technique which predict the prefer direction of one molecule to a second when jump to each other to form a steady compound . Information of the chosen direction in rotate may be worn to expect the strength of involvement or binding affinity linking two molecules with each, for example, score function.

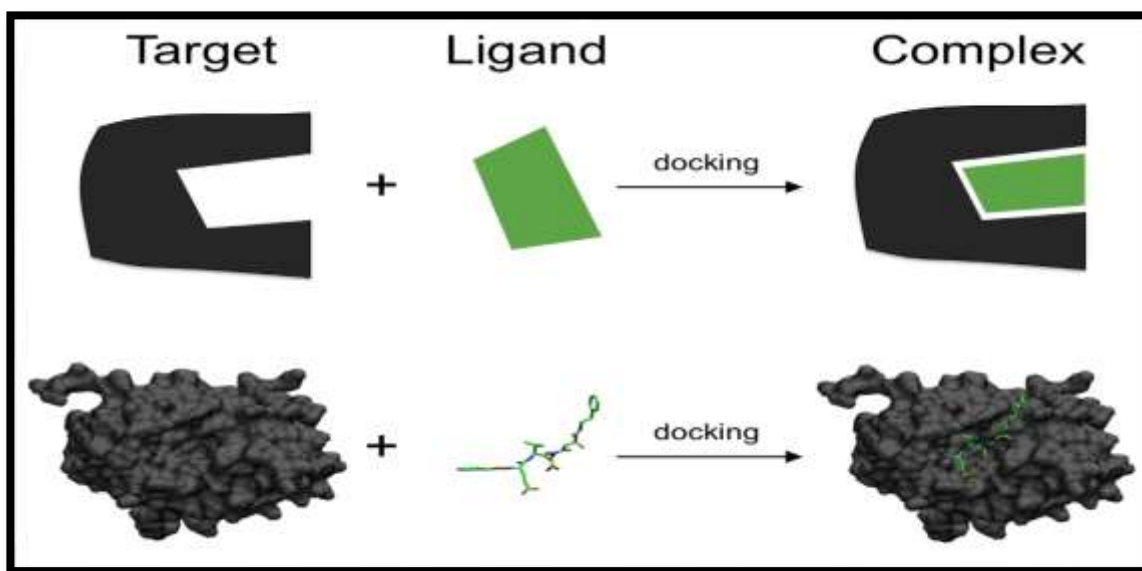


Figure 1 porotine ligand complex

Fig. no 1. Schematic diagram of docking a undersized molecule ligand (green) to a protein target (black) produce a steady compound . The relations between physically appropriate molecules such as proteins, peptides, nucleic acids, carbohydrates, and lipids play a central role in signal transduction. Furthermore, therelative orientation of the two interact associates may involve the type of signal formed (e.g., agonist antagonism).Therefore, docking is helpful for predict both the potency and type of signal produced. Molecular docking is one of the majority generally used technique in structure-based drug design, due to its capability to forecast the binding-conformation of small molecule ligands to the suitable target binding site.^[2] Characterization of the binding performance plays a significant role in rational plan of drugs as well as to explain fundamental biochemical process. The aim of molecular docking is to accomplish an optimized conformation for both the protein and ligand and fundamental direction between protein and ligand so that the free energy of the generally method is minimized. Molecular recognition plays a key role in promote elementary bimolecular proceedings such as enzyme substrate, drug-protein and drug-nucleic acid interactions . Detailed appreciative of the universal principles that administrate the nature of the connections (van der Waals, hydrogen bonding, electrostatic) involving the ligands and their protein or nucleic acid targets may afford a framework for designing the most wanted potency and specificity of potential drug leads for a given therapeutic target . Practical application of this information requires structural data for the goal of significance and a progression for evaluating candidate ligand . A variety of computational docking methods are accessible.^[3]

TYPES OF DOCKING

1. Rigid docking
2. Flexible docking

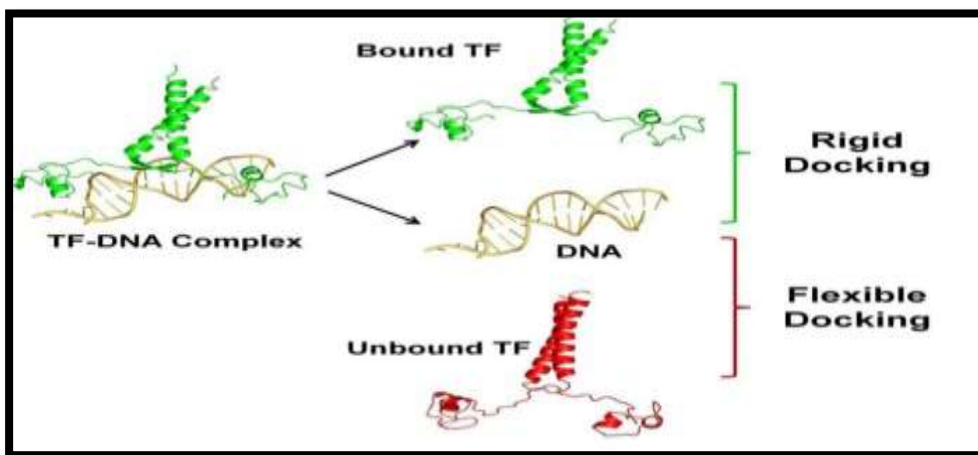
2.1 Rigid Docking

If we think that the molecules are rigid, then we are looking for a conversion in 3D space of one of the molecules which bring it to an most favorable fit with the other molecules in provisions of a scoring function. Conformation of the ligand may be generating in the absence of receptor or in the occurrence of receptor binding activity.^[4]

2.2 Flexible Docking

The molecule flexibility then in adding to transformation, our aspire to locate the confirmations of the receptor and the ligand molecules, as they emerge in complex.^[5]

Figure 1 .DOCKING TYPES



MECHANISM OF DOCKING

1. To achieve a docking screen, the first obligation is an organization of the protein of attention. Typically the structure has been unwavering using a biophysical method such as x-ray crystallography, or less often, NMR spectroscopy. This protein organization and a folder of ligands serve as input to a docking agenda.
2. The success of a docking program depends on two mechanisms such as search algorithm and scoring function. The investigate space consists of all possible orientations and conformations of the protein paired with ligand [complex]. With near computing possessions, it is impossible to comprehensively discover the investigate space this would enumerate all potential distortion of each molecule and all probable rotational and translational orientations of the ligand relation to the protein at an agreed level of granularity.
3. Most docking programs in use account for bendable ligand, and numerous are attempting to model a flexible protein receptor.^[5]
4. Molecular docking is the procedure in which the intermolecular announcement between 2 molecules was studied in in-silico. In this improvement, the macromolecule is the protein receptor. The small particle is the ligand.^[6]
5. Molecule which can be acted as an inhibitor.^[7]

Major Steps Involved in Mechanics of Molecular Docking

So, the docking process involves the following steps:

Step I – preparation of protein

Three-dimensional structure of the protein must be retrieved from Protein Data Bank (PDB); later the retrieved structure should be pre-processed. This should admit amputation of the water molecules from the cavity, stabilize the charges, substantial the missing residue, production the side chains etc. according to the parameter available.^[8]

Step II – active site prediction

After the preparation of protein, the active site of protein must be predicted. The receptor strength possesses lots of active sites merely the one of the concern should be chosen out. Generally the water molecules and hetero atoms are unconcerned if present.^[9]

Step III – preparation of ligand

Ligand can be retrieved from numerous databases such as ZINC, Pub Chem. Or can be sketched

Apply Chem. Sketch tool. While picking out the ligand, the LIPINSKY'S RULE OF 5 should be utilizing. Lipinski rule of 5 assist in discriminating among non-drug like and drug like. The computer-aided drug design and detection (CADD) method. It promises high possibility of achievement or failure due to drug likeness for molecules remaining by with 2 or more than of the complying rules. For choice of a ligand allow to the

Lipinsky's rule

- (1) A lesser amount of five hydrogen bond Donors
- (2) A lesser amount of ten hydrogen bond Acceptors
- (3) Molecular mass less than 500 Da
- (4) High lipophilicity (expressed as Log not Over 5)
- (5) Molar refractivity should be between 40-130.

Step IV Docking: Ligand is docked alongside the protein And the interactions are analyzed.

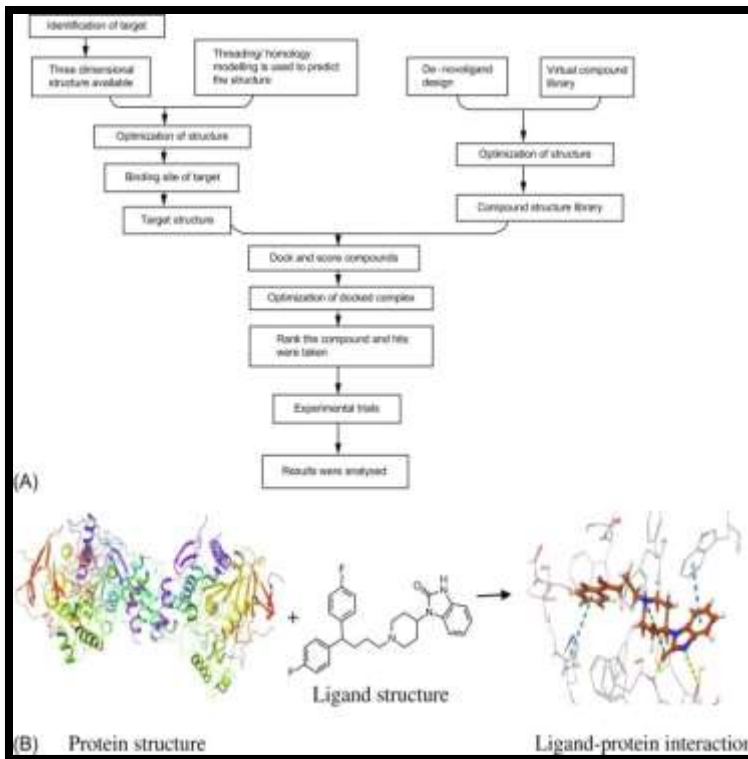


Figure 2 .DOCKING STEPS

Molecular Docking Tools:

In the present work following tooles have been used to carry out the lecular docking of proposed compound.

Tools	Keyfeatures
1.Auto dock tool 1.5.7	3D molecule visualisation, addition of hydrogen, partial atomic charge assignment, grid box setup, result analysis.
2.Pymol	1.To visualize different kinds of moleculessuch as proteins, compounds, or molecules. 2. Save high-quality images in PNG format.
3.Pubchem	1. Served as a central data repository for the NIH's Molecular Libraries Program (MLP) 2. Mostly high-throughput screening (HTS) data from NIH's MLP and other HTS projects. 3.Also contains screening data submitted by data contributors.
4.ResearchCollaboratoryforStructuralBioinformatics (RCSB)	1. The Research Collaboratory for Structural Bioinformatics Protein Data Bank (RCSB PDB)



	2. Information about 3D Dimensional
5. Proteinsplus	1. They are used in Binding site detection 2D interaction diagrams
6. Discovery Studio Visualizer(BIOVIA)	visualization tool for viewing, sharing, and analyzing protein and modeling data.

Table 1 TOOLS FOR MOLECULAR DOCKING

Auto Docking tool

This tutorial will introduce you to docking using the Auto Dock suite of programs. We will use a Graphical User Interface called Auto Dock Tools, or ADT, that helps a user Easily set up the two molecules for docking, launches the external number crunching jobs in Auto Dock, and when the dockings are completed also lets the user interactively visualize the docking results in 3D.

Application of Auto Dock tool

1. Auto Dock is a molecular modeling simulation software. It is particularly effective for Protein-ligand docking.
2. Auto Dock is one of the most cited docking software applications in the research Community.
3. Auto Dock software consists of two programs, Auto Grid and among them, Auto Grid is mainly responsible for the calculation of relevant energy in the grid, while Auto Dock is responsible for conformation search and evaluation.
4. Auto Dock runs on Linux, Mac OS X, SGI IRIX and Microsoft Windows. It is available as a package on several Linux distributions, including Debian, Fedora, and Arch Linux.
5. Auto Dock includes but is not limited to, the following applications: X-ray Crystallography, structure-based drug design, lead compound optimization, virtual Screening, combinatorial library design, protein-protein docking, and chemical Mechanism studies.

Ligand preparation steps

1. Draw your ligands using a Java applet, upload a single ligand file or multiple ligands.
2. Draw chemical structures by Marvin Sketch, a Java based program with a constantly Growing list of editing features and a number of templates to make molecule drawing simpler.
3. Upload a ligand in MDL MOL, SYBYL MOL2, PDB, HYPERCHEM HIN or SMILES Format.
4. Upload multiple ligands in SDF format you can set various parameters during the Simulation such as desired PH, structure optimization and partial charge calculations using. Molecular mechanics or semi empirical quantum chemical methods.
5. Set up rotatable bonds and atom types automatically or modify manually Download the attached files in several file formats including mol, pdb, mol2 and pdbqt. Organize your ligands into self-defined folder.^[10]

Molecular Docking for Benzimidazol & Clorobiocin

• Drug information of Benzimidazol:

- Benzimidazole is a heterocyclic organic compound with the molecular formula C₇H₆N₂. It consists of a bicyclic ring system containing benzene and imidazole rings fused together. Benzimidazole and its derivatives have diverse pharmacological properties and are used in the development of various drugs. Some pharmacological actions are anti paracitic, Antineoplastic, Antiviral, Anthelminthic Agent, Antifungal Agent, Proton Pump Inhibitor etc.^[11]

**Figure 4 USES OF BENZIMIDAZOL WITH STRUCTURE**

- Molecular Weight Approximately 118.14g/mol
- **Drug information Clorobiocin:** Clorobiocin is a potent antibiotic derived from *Streptomyces roseochromogenes*. It belongs to the aminocoumarin class of antibiotics and is structurally similar to novobiocin. Clorobiocin inhibits bacterial DNA gyrase, which is essential for bacterial DNA replication, thus exerting its antibacterial effects. It has shown activity against a wide



range of Gram-positive and some Gram-negative bacteria. However, its clinical use has been limited due to its toxicity profile and thavailability of alternative antibiotics.

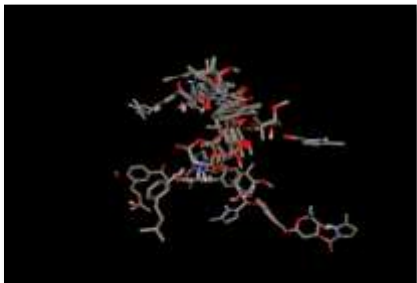


Figure 3 3D IMAGE OF PDB ID 1KZN



Figure 4 2D IMAGE OF PDB ID 1KZN

RECEPTOR AND LIGAND PROFILE:

PDB DOI: <https://doi.org/10.2210/pdb1KZN/pdb>

Classification: ISOMERASE

Organism(s): *Escherichia coli*

Expression System: *Escherichia coli*

Receptor name: E. coli 24kDa Domain in Complex with CLOROBIOCIN

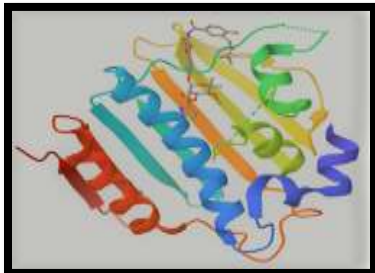


Figure 5: E. coli 24kDa Domain in Complex with CLOROBIOCIN

- Method: X-RAY DIFFRACTION
- Resolution: 2.30 Å
- R-Value Free: 0.267
- R value work:0.289

Ligand profile



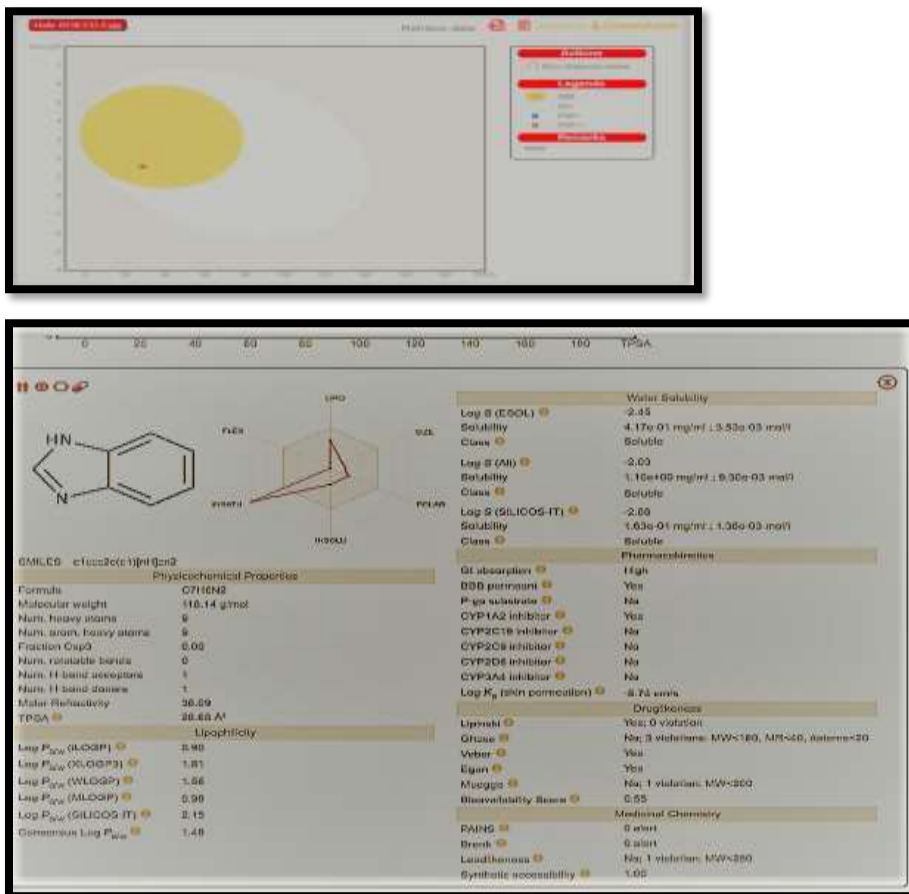
Pubchem CID:5798

Drug name: Benzimidazol

Classification : heterocyclic aromatic organic compound

Molecular formula: $C_7H_6N_2$

IUPAC Name: 1*H*-benzimidazole

**Figure no 6. SWISSADME**

METHODS

Autodock vina

Autodock vina is An open supply application for doing molecular docking .it became designed and Carried out via Way of means of Dr.oleg trot in the molecular Graphics Lab at The scripps Research Institute. Autodock vina notably improves the common accuracy of the binding mode predictions as compared to Autodock .jldging via way of means of the checks at the education set utilized in autodock development.

Target preparation

For the docking purpose, receptor preparation is essential step. Receptor –ligand complex formation is required for the pharmacological activity. For this study purpose the receptor which is E. coli 24kDa Domain in Complex with CLOROBIOCIN selected from litreture survy. By the inhibition action on this given receptor may prevent the progress of disease.^[12]

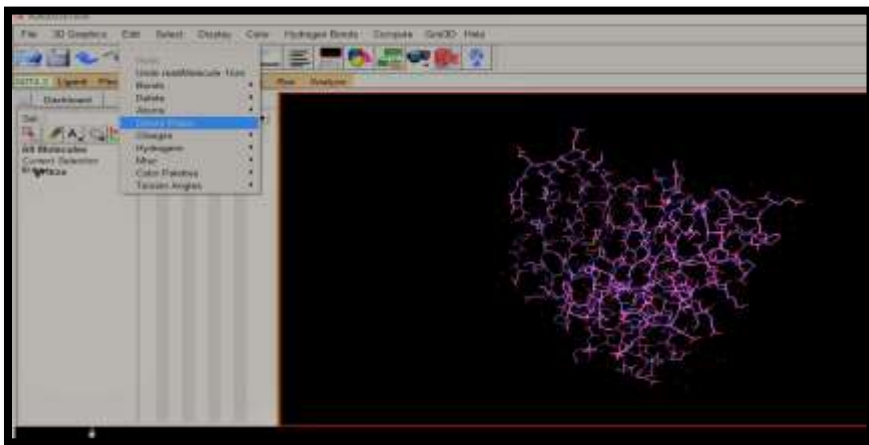


Figure 7. RSCB database with PDB- ID -1kzn

For the docking study the receptor should be in PDBQT formats, so that can be converted by following steps by using Autodock tools.

A) Protine preparation

1. Open the PDB format of receptor 1kzn in Auto dock Vina by clicking vina by clicking 'file In subsection read molecule.
2. Go to Edit & Deleting Water molecule, select from string as shown in fig:



Figureno. 8. delete water molecule in Autodock vina

- 3) Then go to select & click on select from string and add Hetatm as show in Fig:

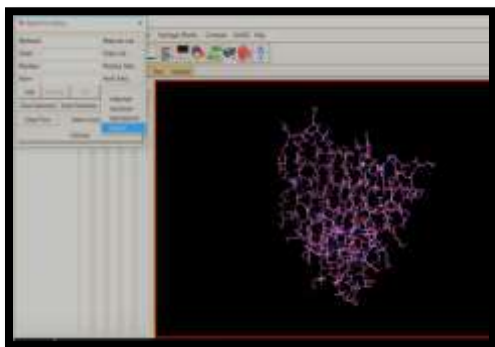


Figure 9.Add hetam

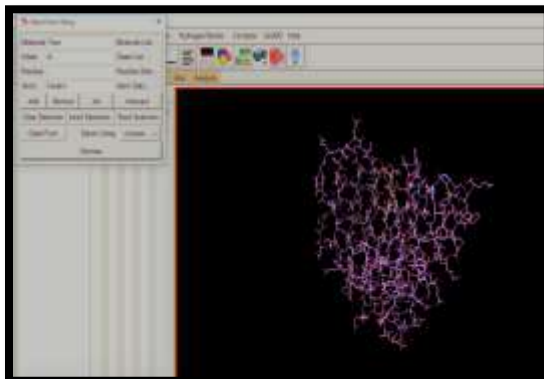


Figure no. 11 select from string

4) Then go to edit and click on Delete Selected Atoms as shown in Fig:

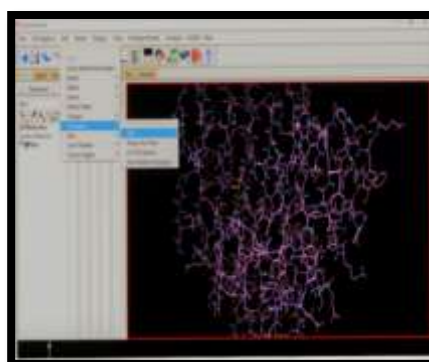
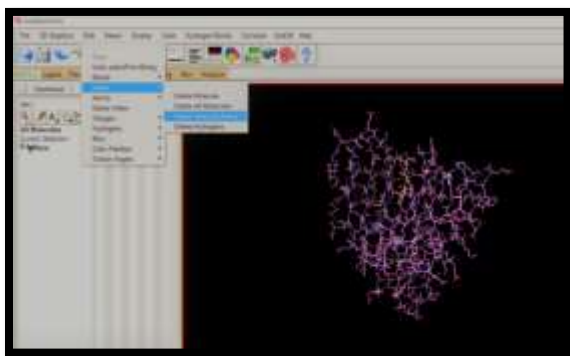


Figure 10..delete selected atoms

5)Then go to edit and click on “add hydrogen (polar only) as show in Fig:

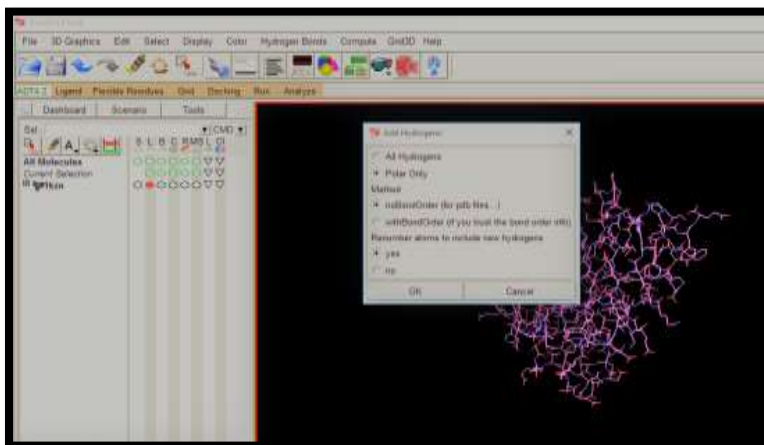


Figure 11.add hydrogen polar only



6) Then go to edit and “add kollman charges” as shown in fig:

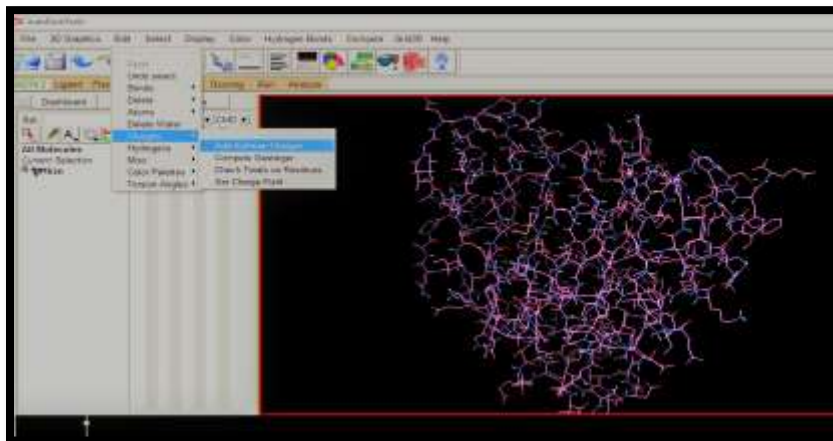


Figure 12.Add kollam charges

7) Then go to edit and click on atoms chose “Assign AD4 type”.as shown in the fig

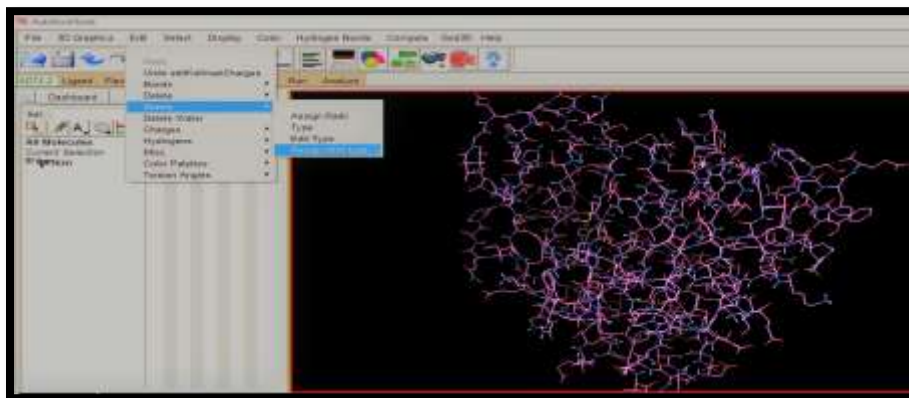


Figure 13.Assing AD4 type

8) Then go to the file section and save bottom then select PDBQT format to save select the END and add molecule, as shown in Fig:

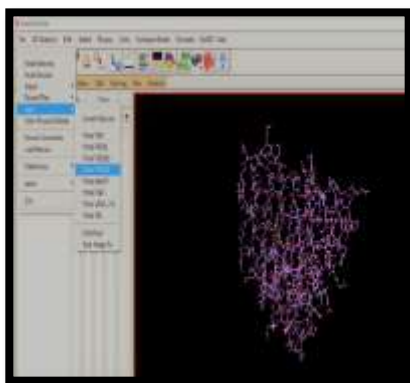


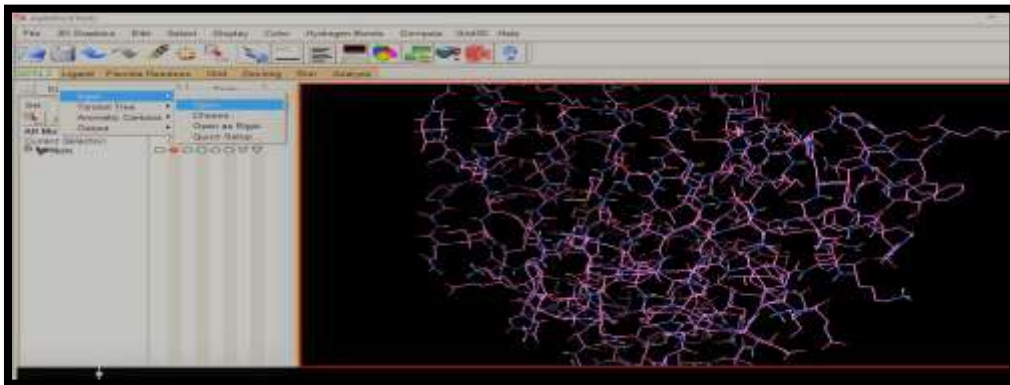
Figure 17.select PDBQT Formate.



Figure 14.select END &save

B)Ligand preparation

1. Click the ligand section then choose input add click on the open option.as shown in fig:

**Figure 15.choose input add & open**

2)After loading the molecule click the on-torsion tree under the same ligand section and click on choose root then detect root as shown in fig.

**Figure 16.torsion tree choose root****Figure 17.detect root**

3. Then go to the output option and save it in PDBQT format.

C) Grid generation

1. Open PDBQT of 1kzn receptor which is saved in an earlier step. Then the grid and choose And choose a receptor as a macromolecule. Then select the 1kzn receptor molecule and click No for reserve change as shown in fig:

**Figure no 22 : choose receptor as macromolecule.**



2. Then click on Set map types and choose ligand as shown in fig .

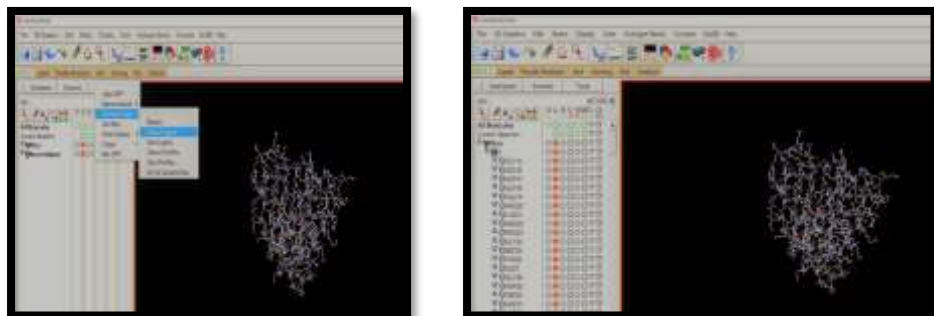


Fig 23. Set map types & choose ligand

3. Then in the grid section, click on the grid box as shown in Fig:

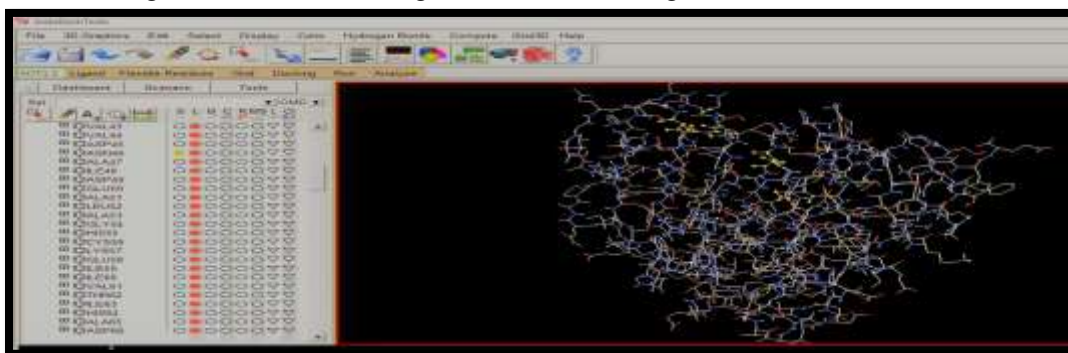


Fig 24. grid section

4. Then click on the grid box Adjust the grid box using the grid box coordinates so that the Receptor molecule is enclosed within the box then click the button in the grid option and Select “output grid dimension file” as shown in Fig:

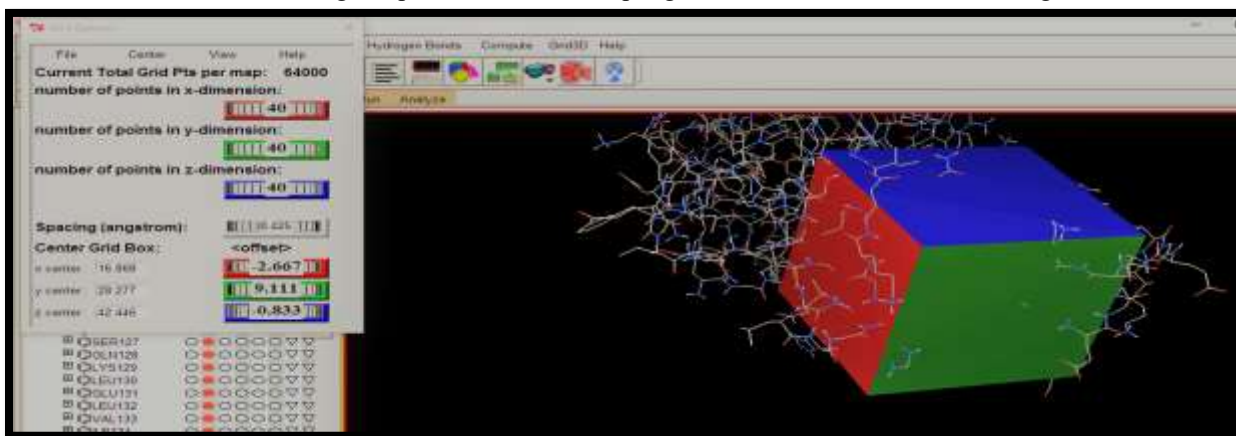


Figure 25 : output grid dimension file



D) Config file:

1) Open a new document file and enter the configuration details of the grid box, receptor name, ligand name, energy range and exhaustiveness as given in picture not as shown in Fig:

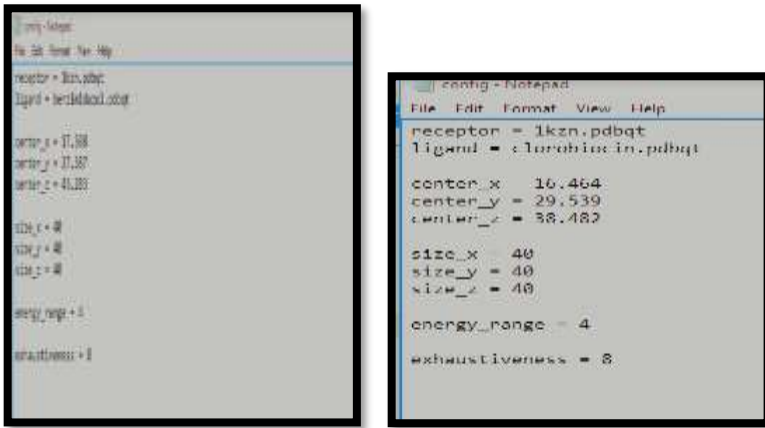


Fig.no 26: Config File of test & standard drug

E) Command Prompt:

- 1) Search for command prompt in your laptop or computer
- 2) Then enter, followed by 'cd' Paste the folder location in which all require are present them press enter as shown in Fig:

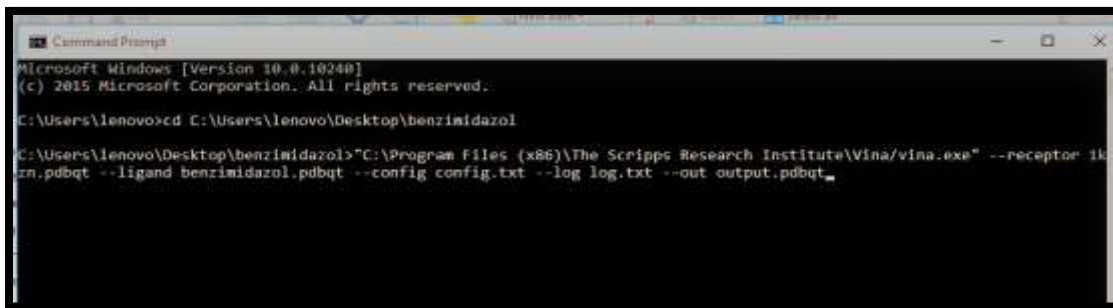


Fig no.27 Command Prompt

3) Then run docking vina copy address "vina search-receptor 1kzn,, pdbqt –ligand benzimidazol.pdbqt – configconfig .txt-log log .txt- out output.pdbqt as shown in Fig:



4) After that it will take some time and give us the result of docking as shown in Fig:

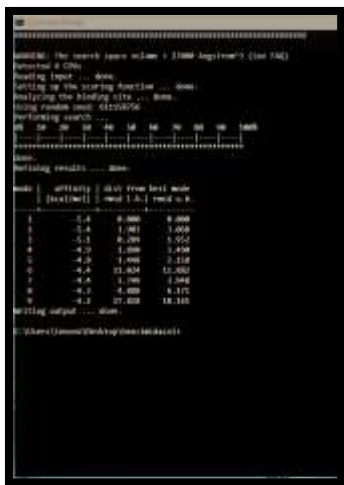


Figure no 28 .result of test drug



Figure no 29. Result of standard drug

5) Then Output file of the result will automatically save in the command folder, which can be Read by using notepad.

Result Docking

Docking Result of Benzimidazol

The result of test drug Benzimidazol and their target microorganism, PDB ID binding energy and standard drug like Clorobiocin for comparative study have been summarised as below table by autodockvina tool

Sr.no	Target Name	Microorganism Name	PDB ID	Binding energy of Test drug	Binding energy of Standard Drug
1	DNA gyrase inhibitors	Escherichia Coli	1KZN	-5.4	-7.9

For Visualization of Docking result

1 For the visualization of result we use “Discovery Studio BIOVIA” Terminal look like as shown in the fig.

2 open out file obtained from Docking by click on file section. Then delete all poses by clicking on it except best pose which will be 1 in all cases.

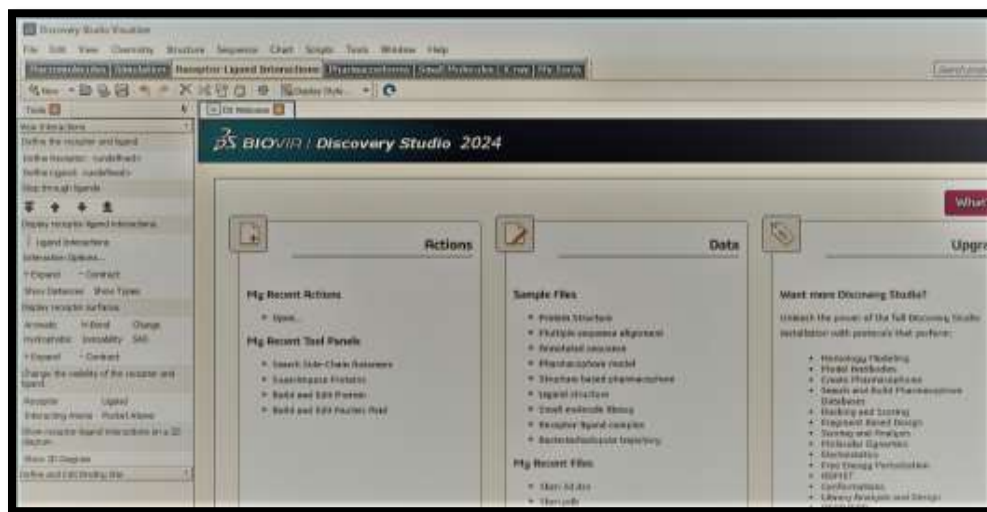


Fig. No 30. Terminal of Discovery Studio BIOVIA



3. Now go to file section and open 1KZN receptor PDBQT file in new terminal of biovia software. From this terminal copy receptor & paste it in ligand terminal.



Fig no. 31. Complex of ligand with receptor with suitable pose

4. After define receptor & ligand from the complex, then click on “ligand receptor complex” .



Fig no. 32. ligand interaction option

5. In Show ‘receptor ligand interaction in 3d diagram, click on show, 3D Diagram’. Where you will get image of amino acids attached to ligand in 3D formate.

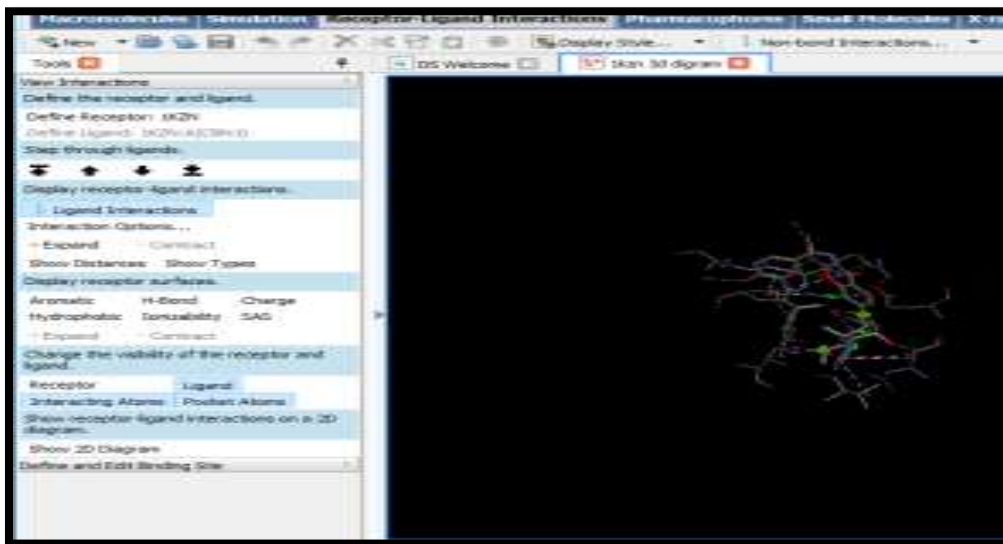


Fig no. 33. 3D image of ligand & receptor complex

6. In Show receptor ligand interaction in 2D Diagram, click on show 2D diagram'. where you will get image of amino acids attached to ligand in 2D format.

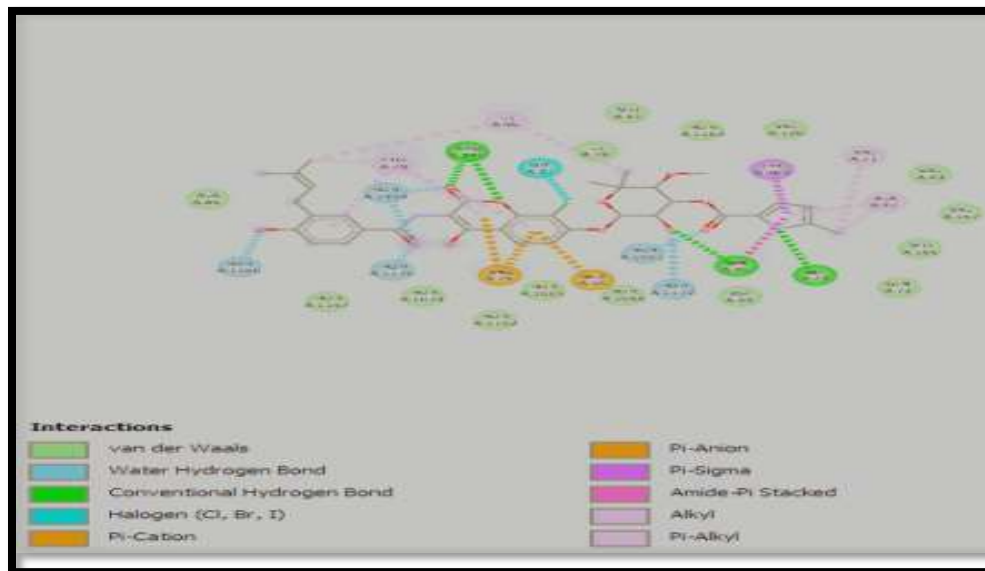


Fig no. 34 2D image of ligand & receptor complex

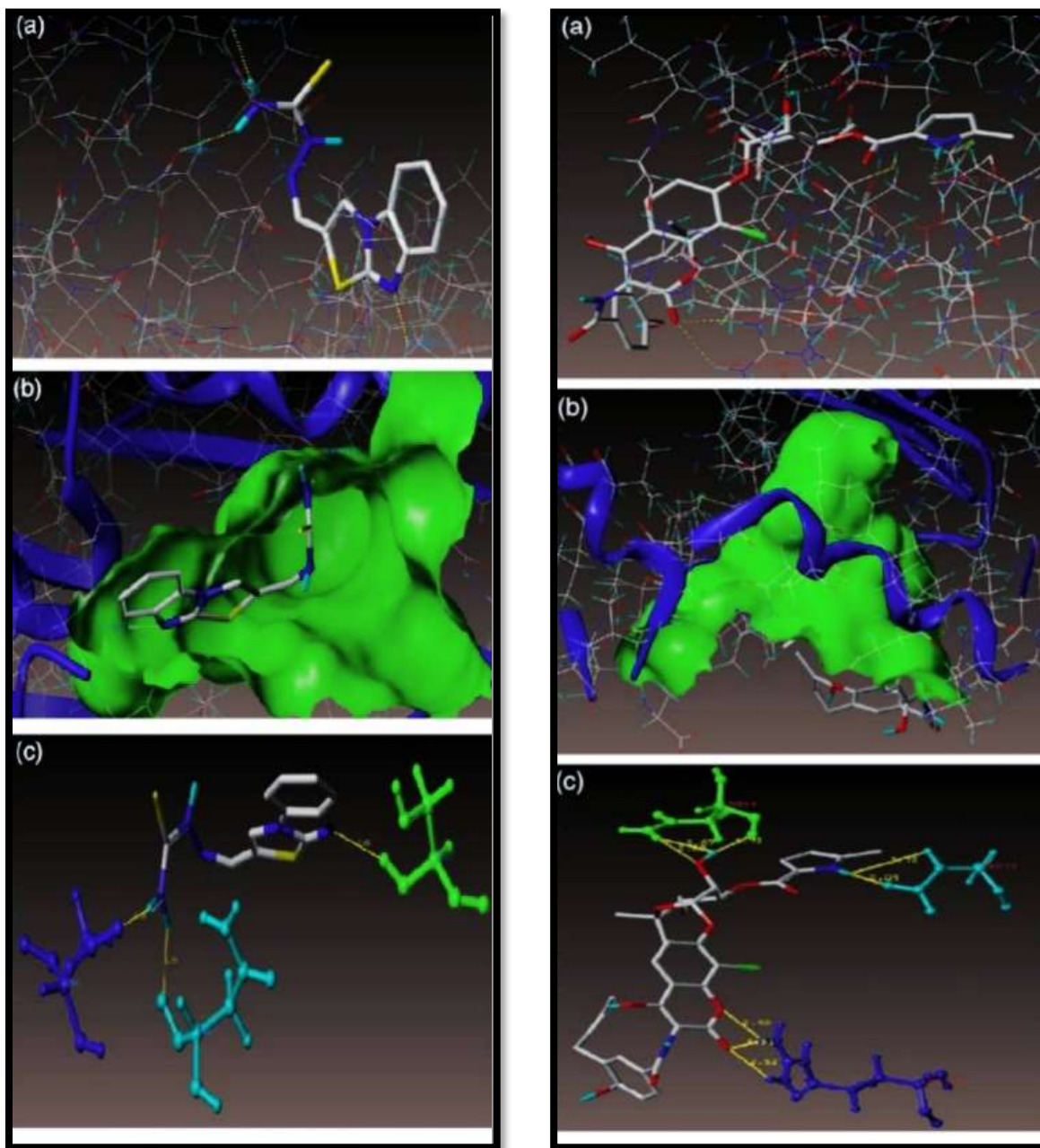


Figure no. :35 Interaction of compound at binding site of enzyme & Docked view of clorobiocin(std drug) at active site of enzyme PDB ID:1KZN respectively

DISCUSSION

Molecular docking studies have been performed on Benzimidazol and clorobiocin to understand their binding mechanisms and potential interactions with target proteins Beyond its pharmaceutical importance, benzimidazole demonstrates its versatility across diverse domains, including materials science and awide spectrum of pharmacological applications, encompassing antiviral, antifungal, antioxidant, and anticancer properties..Clorobiocin is aminocoumarin antibacterial that inhibits the enzyme DNA gyrase.Molecular docking of benzimidazole and clorobiocin sounds like an interesting project! Molecular docking is a powerful tool used in drug discovery



to predict the binding interactions between a small molecule (like benzimidazole) and a target protein (perhaps an enzyme inhibited by clorobiocin). Here are some points we could discuss: Purpose of the Study: Docking Protocol: Describe your docking protocol. How are you preparing the protein (e.g., adding missing atoms, charges, etc.)? What parameters are you using for the docking simulations? Analysis of Results: How will you analyze the docking results? Are you focusing on binding affinities, specific interactions, or binding poses? Visualization tools like PyMOL or Chimera can be helpful. Significance and Implications: What are the potential implications of your findings? Could they guide future drug design efforts or provide insights into structure-activity relationships? Challenges and Limitations: Have you encountered any challenges during the project? Docking studies can be sensitive to parameters like grid size, scoring functions, and ligand flexibility:

CONCLUSION

The conclusion of a molecular docking study involving benzimidazole and clorobiocin would typically summarize the findings and implications of the study. Here's a sample conclusion based on potential outcomes: "The molecular docking study of benzimidazole and clorobiocin revealed promising interactions between these compounds, suggesting potential binding at specific target sites. Clorobiocin demonstrated favorable binding affinity with key residues in the active site of the target protein, indicating its potential as a competitive inhibitor. Benzimidazole also exhibited notable interactions, albeit with differing binding modes. These findings suggest a basis for further exploration of these compounds as potential leads for drug development targeting specific biological pathways. "In summary, molecular docking can be a useful tool for understanding the potential interactions between mefenamic acid and ampicillin with target proteins, which can provide insights into their mechanisms of action and potential therapeutic applications.

REFERENCE

1. Wong K.C. A novel approach to predict core residues on cancer-related DNA-binding domains. *Cancer Inf.* 2016;15:1-7. [PMC free article] [PubMed] [Google Scholar]
2. Arunan E.; Desiraju G. R.; Klein R. A.; Sadlej J.; Scheiner S.; Alkorta I.; Clary D. C.; Crabtree R. H.; Dannenberg J. J.; Hobza P.; Kjaergaard H. G.; Legon A. C.; Mennucci B.; Nesbitt D. J. Definition of the Hydrogen Bond (IUPAC Recommendations 2011). *Pure Appl. Chem.* 2011, 83 (8), 1637-1641. 10.1351/PAC-REC-10-01-02. [CrossRef] [Google Scholar]
3. Vijayan, R. S. K.; Kihlberg, J.; Cross, J. B.; Poongavanam, V. Enhancing preclinical drug discovery with artificial intelligence. *Drug Discovery Today* 2022, 27 (4), 967- 984, DOI: 10.1016/j.drudis.2021.11.023
4. Guedes IA, Pereira FSS, Dardenne LE. Empirical scoring functions for structure-based virtual screening: Applications, critical aspects, and challenges. *Frontiers in Pharmacology.* 2018;9:1089
5. Wiesmann C, Barr KJ, Kung J, Zhu J, Erlanson DA, Shen W, Fahr BJ, Zhong M, Taylor L, Randal M, McDowell RS, Hansen SK. Allosteric inhibition of protein tyrosine phosphatase 1B. *Nature Structural and Molecular Biology.* 2004;11:730-737. [PubMed] [Google Scholar]
6. Morris GM, Goodsell DS, Halliday RS, Huey R, Hart WE, Belew RK, Olson AJ. *J Comput Chem.* 1998;19:1639. doi: 10.1002/(SICI)1096-987X(19981115)19:14<1639::AID-JCC10>3.0.CO;2-B. [CrossRef] [Google Scholar]
7. Matenia D.; Mandelkow E.-M. The Tau of MARK: A Polarized View of the Cytoskeleton. *Trends Biochem. Sci.* 2009, 34, 332-342. 10.1016/j.tibs.2009.03.008. [PubMed] [CrossRef] [Google Scholar]
8. Morris GM, Goodsell DS, Halliday RS, Huey R, Hart WE, Belew RK, Olson AJ (1998) *J Comput Chem* 19:1639
9. Si, J.; Zhang, Z.; Lin, B.; Schroeder, M.; Huang, B. MetaDBSite: A meta approach to improve protein DNA-binding sites prediction. *BMC Syst. Biol.* 2011, 5, S7. [Google Scholar] [CrossRef] [Green Version]
10. de Sousa JMA (2017) Processing of SMILES, InChI, and Hashed Fingerprints. In: Varnek A (ed) *Tutorials in chemoinformatics.* Wiley, Chichester, pp 75-81
11. Aroua L. M., Almuhaylan H. R., Alminderej F. M., Messaoudi S., Chigurupati S., Al-Mahmoud S., et al. (2021). A facile approach synthesis of benzoylaryl benzimidazole as potential α -amylase and α -glucosidase inhibitor with antioxidant activity. *Bioorg. Chem.* 114, 105073. 10.1016/j.bioorg.2021.105073 [PubMed] [CrossRef] [Google Scholar]
12. Patil RB, Sawant SD. Synthesis, characterization, molecular docking and evaluation of antimicrobial activity of some 3-heteroaryl substituted chromen-2-one derivatives. *Int J Pharm Tech Res* 2014. 2015;7(3):471-480. [Google Scholar]